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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/767,215	01/22/2001	John Bertin	07334-142001/ MPI2000-003	3061

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EXAMINER
DAVIS, MINH TAM B

ART UNIT	PAPER NUMBER
1642	15

DATE MAILED: 02/12/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/767,215	BERTIN, JOHN	
	Examiner	Art Unit	
	MINH-TAM DAVIS	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 November 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8 and 21-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8 and 21-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *11* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Effective February 7, 1998, the Group Art Unit location has been changed, and the examiner of the application has been changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Minh-Tam Davis, Group Art Unit 1642.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Applicant cancels non-elected claims 9-20, and adds new claims 21-34, which are related to claims 1-8, and are not new matters.

Accordingly, claims 1-8, 21-34 are being examined.

Claims 1-2, 29-32 seem to be free of prior art and are allowable.

The following are the remaining rejections.

Claim Rejections - 35 USC § 112, FIRST PARAGRAPH, WRITTEN DESCRIPTION, NEW REJECTION

Claims 3-8, 21-28, 33-34 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 3-8 are drawn to a polypeptide "comprising" at least 25, 50, 100, 200, 400, or 600 contiguous amino acids of the amino acid sequence of SEQ ID NO:2

(CARD-14). Claims 21-25 are drawn to a polypeptide "comprising" amino acids 10-116, 126-420, 568-660, 676-745, or 826-1004 of SEQ ID NO:2. Claims 26-28 are drawn to an amino acid sequence that is at least 85%, 95% or 98% identical to SEQ ID NO:2, wherein said amino acid sequence binds to Bcl-10. Claim 33 is drawn to a fusion polypeptide "comprising" at least 25 contiguous amino acids of the amino acid sequence of SEQ ID NO:2, which is linked by a peptide bond to a heterologous polypeptide. Claim 34 is drawn to a fusion polypeptide "comprising" amino acids 10-116, of SEQ ID NO:2, which is linked by a peptide bond to a heterologous polypeptide.

Claims 3-8, 33 encompass unrelated amino acid sequences of any length and any structure, provided they contains at least 25, 50, 100, 200, 400, or 600 contiguous amino acids of the amino acid sequence of SEQ ID NO:2. Claims 21-25, 34 encompass unrelated amino acid sequences of any length and any structure, provided they contain amino acids 10-116, 126-420, 568-660, 676-745, or 826-1004 of SEQ ID NO:2. Claims 26-28 encompass variants of SEQ ID NO:2, wherein the function of said variant is unknown, because binding to Bcl-10 is not a function.

The specification discloses that CARD-14 associates with Bcl-10 via the N terminal CARD domain (p.21 and p.22, first paragraph). The specification also discloses that the N-terminal CARD of CARD-14 was essential for NF-kB signaling (p.24). No disclosure however is found in the specification whether the N-terminal CARD by itself is sufficient for activating NF-kB.

The specification also discloses proteins that have an amino acid sequence at least about 45%, preferably 55%, 65%, 75%, 85% , 95% or 98% identical to SEQ ID

NO:2 and retains the functional activity of SEQ ID NO:2 (p.38, lines 13-16). The specification further discloses a nucleic acid sequence encoding a protein that is at least 45%, 55%, 65%, 75%, 85% , 95% or 98% identical to SEQ ID NO:2 (p.32, second paragraph).

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).

Although drawn to nucleic acids, the teaching of *The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412) is clearly relevant to the instant rejection. The court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by

structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

The instant specification fails to provide sufficient descriptive information, such as definitive strutural or functional features of the claimed genus of polypeptides. Further, the claims read on variants of SEQ ID NO:2, wherein said variants have any type of substitution besides conservative substitution, at any amino acid, throughout the length of SEQ ID NO:2, as well as insertions and deletions. The specification and the claims do not place any limit on which amino acid to be subjected to conservative or non-conservative substitution, the type of substitution besides conservative substitution, nor the type of amino acids replacing the original amino acids. In addition, the specification and all other pending claims do not place any limit on the number of amino acids that could be substituted, deleted or added, provided the upper limit of the variation is 15%, 5% or 2%. Thus the scope of the claims includes numerous structural variants. Although the types of changes are routinely done in the art, the specification and the claims do not provide any guidance as to which, or how many original amino acid(s) to be substituted, or to which type of substitution besides conservative substitution, or which amino acids could be deleted or inserted so that the claimed polypeptide could function as contemplated. No common structural attributes that identify the claimed variants are disclosed. In addition, no common functional attributes that identify the claimed variants are disclosed, because the function of a polypeptide sequence could be abolished, even with substitution of only one amino acid of the polypeptide (Burgess et al. Journal of Cell Biology, 1990, 11: 2129-2138). The general knowledge and level of skill in the art do not

supplement the omitted description, because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the claimed variants, SEQ ID NO:2 alone is insufficient to describe said variants. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of variants. Thus, applicant was not in possession of the claimed variants.

Thus, there is insufficient support of claims 3-8, 21-25, 26-28, 33-34 as provided by the Interim Written Description Guidelines published in the June 5, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645. Therefore, only SEQ ID NO:2, but not the full breadth of the claims meets the written description provision of 35 USC 112, first paragraph.

Claim Rejections - 35 USC § 112, FIRST PARAGRAPH, SCOPE

If Applicant could overcome the above 112, first paragraph rejection, claims 26-28 are still rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for SEQ ID NO:2, does not reasonably provide enablement for variants of SEQ ID NO:2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 26-28 are drawn to an amino acid sequence that is at least 85%, 95% or 98% identical to SEQ ID NO:2, wherein said amino acid sequence binds to Bcl-10.

The scope of the claims 26-28 includes numerous structural variants. Applicants have not shown how to make and use the claimed polypeptide variants which are capable of functioning as that which is being disclosed.

Protein chemistry is probably one of the most unpredictable areas of biotechnology.. For example, replacement of a single lysine residue at position 118 of acidic fibroblast growth factor by glutamic acid led to the substantial loss of heparin binding, receptor binding and biological activity of the protein (Burgess et al. Journal of Cell Biology, 1990, 11: 2129-2138). In transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen (Lazar et al. Molecular and Cell Biology, 1988, 8: 1247-1252). Similarly, it has been shown that aglycosylation of antibodies reduces the resistance of the antibodies to proteolytic degradation, while CH2 deletions increase the binding affinity of the antibodies (see Tao. et al. The Journal of Immunology, 1989, 143(8): 2595-2601, and Gillies et al. Human Antibodies and Hybridomas, 1990, 1(1): 47-54). These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification will often dramatically affect the biological activity and characteristic of a protein.

In view of the above unpredictability, one of skill in the art would be forced into undue experimentation in order to perform the claimed invention as broadly as claimed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 703-305-2008. The examiner can normally be reached on 9:30AM-4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, ANTHONY CAPUTA can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0916.

ANTHONY C. CAPUTA
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

MINH TAM DAVIS

January 30, 2003